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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/088,598	03/21/2002	Akio Yamane	2002-0401A	6872

513 7590 10/04/2004

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EXAMINER	
SAKELARIS, SALLY A	

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 10/04/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/088,598	YAMANE, AKIO	
	Examiner	Art Unit	
	Sally A Sakelaris	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 July 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3 and 5-9* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3 and 5-9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☒ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This action is written in response to applicant's correspondence submitted 7/22/2004. Claims 1 and 5 have been amended, claim 4 has been canceled, and no claims have been added. Claims 1-3 and 5-9 are pending. Applicant's amendments and arguments have been thoroughly reviewed, but are not persuasive for the reasons that follow. Any rejections not reiterated in this action have been withdrawn as necessitated by applicant's amendments to the claims. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. **This action is FINAL.**

Priority

Acknowledgement of claim to foreign priority of Japanese Application, 11/268745, filed 9/22/1999 under 35 U.S.C. 119(a)-(d) has been made, however applicant should note that the certified copy and translation of this foreign priority document has not yet been received and as a result the claim to foreign priority under the same has not yet been granted.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

1. Claims 1-9 are rejected under 35 U.S.C. 102(b) as being anticipated by Livak et al.(US Patent 5,723,591)

With regard to claim 1, Livak et al. teach a probe comprising a nucleic acid carrying a labeling substance that releases energy and an energy-absorbing substance capable of absorbing the energy(quencher) released from the labeling substance, wherein energy transfer from the labeling substance to the energy-absorbing substance is intercepted by the hybridization of the probe with a target nucleic acid, in their teaching of an oligonucleotide probe "which includes a fluorescent reporter molecule and a quencher molecule capable of quenching the fluorescence of the reporter molecule"(abstract and for example Figure 1 and claim 1). The reference goes on to teach that "the oligonucleotide probe is constructed such that the probe exists in at least one single-stranded conformation when unhybridized where the quencher molecule is near enough to the reporter molecule to quench the fluorescence of the reporter molecule". "The oligonucleotide probe also exists in at least one conformation when hybridized to a target polynucleotide where the quencher molecule is not positioned close enough to the reporter molecule to quench the fluorescence of the reporter molecule"(Abstract).

With regard to claim 2, Livak et al. teach that "the reporter molecule and quencher molecule are positioned on the probe sufficiently close to each other such that whenever the reporter molecule is excited, the energy of the excited state nonradiatively transfers to the quencher molecule where it either dissipates nonradiatively or is emitted at a different emission frequency than that of the reporter molecule"(Col. 3 lines 3-8).

With regard to claim 3, Livak et al. teach that the labeling substance is a fluorescent substance and "may be selected from xanthene dyes, including fluoresceins, and rhodamine dyes"(Col. 11 lines 22-23).

With regard to claims 4 and 5 Livak et al. teach that the energy absorbing(quencher) is an intercalator or a substance which specifically binds to a double stranded nucleic acid, in Col. 11 in their teachings of exemplary reporter-quencher pairs and dyes including acridines like acridine orange, "pyrenes and the like"(lines 33-35).

With regard to claim 6, Livak et al. teach that the labeling substance "may be selected from xanthene dyes, including fluoresceins, and rhodamine dyes"(Col. 11 lines 22-23). While Livak et al. also teach that the energy absorbing(quencher) may be selected from another group of fluorescent compounds including acridines like acridine orange, "pyrenes and the like"(lines 33-35).

With regard to claim 7, Livak et al. teach "according to one embodiment of the method, the hybridization probe is immobilized on a solid support"(Col. 8, lines 38-50). "The oligonucleotide probe is contacted with a sample of nucleic acids under conditions favorable for hybridization". "The fluorescence signal of the reporter molecule is measured before and after being contacted with the sample. Since the reporter molecule on the probe exhibits a greater fluorescence signal when hybridized to a target sequence, an increase in the fluorescence signal after the probe is contacted with the sample indicates the hybridization of the probe to target sequences in the sample". "Immobilization of the hybridization probe to the solid support enables the target sequence hybridized to the probe to be readily isolated from the sample"(Col. 8 and claim 16).

With regard to claims 8 and 9, as stated above, Livak et al. teach that "the present invention relates to the use of the oligonucleotide probe as a hybridization probe to detect target polynucleotides"(Col. 5 lines 39-60). Further that "quantification of the change in fluorescence

intensity as a result of the probe being contacted with the sample can be used to quantify the amount of target sequences present in the sample"(Col. 5 lines 55-58).

Response to Arguments

Applicant's arguments filed 7/22/2004 have been fully considered but they are not persuasive. Applicant first argues that Livak et al. "fails to disclose or suggest each and every element of the claimed invention, namely a probe comprising an intercalator or an energy-absorbing substance that specifically binds a double stranded nucleic acid due to the hybridization of the probe with a target nucleic acid whereby the energy transfer from the labeling substance to the energy-absorbing substance is intercepted resulting in no quenching"(6/30/04 response pg. 5). Applicant should note that this limitation is not recited in their claims as they are presently written. Limitations in applicant's arguments, specification etc cannot be read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Furthermore, without a requirement for the interception to result in no quenching, or a requirement for a hybridization step to necessitate the interception, the art will be applied as broadly as the claims are written. The courts have stated that claims must be given their broadest reasonable interpretation consistent with the specification *In re Morris*, 127 F.3d 1048, 1054-55, 44 USPQ2d 1023, 1027-28 (Fed. Cir. 1997); *In re Prater*,415 F.2d 1393, 1404-05, 162 USPQ 541, 550-551 (CCPA 1969); and *In re Zletz*, 893 F.2d 319, 321-22, 13 USPQ2d 1320, 1322 (Fed. Cir. 1989) (see MPEP 2111). As such, one interpretation of the claim is that the quencher moiety is intercepting the energy transfer from the labeling substance. It should further be noted that the requirement for an intercalator is made in the alternative and as such is not a required limitation to be taught in the cited art.

Next, applicant argues that in the specification on page 5, lines 3-9, discusses the fact that "the energy transfer from the labeling substance to the energy-absorbing substance or intercalator

is intercepted by the hybridization of the probe with a target nucleic acid". "This, in turn, releases the light from the labeling substance" and further that reference to the specification at page 8, lines 11-29 and also in Figure 1 teach the embodiment of their invention that is not taught by the prior art. However, it is maintained that limitations of the specification shall not be read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). It should be further noted that if applicants do amend their claims to include, thus far unexamined limitations, further search and examination would be required.

Lastly applicant argues that Livak "neither discloses nor suggests that a quencher molecule binds to or intercalates to a double-stranded nucleic acid or that the fluorescence of the reporter molecule in thereby unquenched". However, as stated above this limitation is not in the claims as presently written and furthermore there is no requirement in the claim for the ordered sequential steps of hybridization, intercepting, and quenching to occur which applicant argues in their response. Furthermore, the fact that the Livak probe includes a conformational change is irrelevant considering the claim does not preclude such an embodiment and further that Livak is able to anticipate the limitations of the claims as presently written.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after

the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sally A Sakelaris whose telephone number is 571-272-0748. The examiner can normally be reached on M-Fri, 9-6:30 1st Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Sally Sakelaris
9/30/04

GARY BENZION
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